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CONFIRMATION BY MAIL ☐

INTERNATIONAL COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: GREGORY D. WILLIAMS
NEW ENGLAND BIOLABS, INC.
32 TOZER ROAD
BEVERLY, MASSACHUSETTS 01915

PCT

NOTIFICATION OF TRANSMITTAL OF
INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

RECEIVED
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Date of Mailing
(day/month/year)

03 OCT 2001

Applicant's or agent's file reference

NEB-163-PCT

IMPORTANT NOTIFICATION

International application No.

PCT/US00/14122

International filing date (day/month/year)

23 MAY 2000

Priority Date (day/month/year)

24 MAY 1999

Applicant:

NEW ENGLAND BIOLABS, INC.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301)

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks
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Washington, D.C. 20231

Authorized officer

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Form PCT/IPEA/416 (July 1992) *

TENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

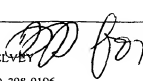
Applicant's or agent's file reference NEB-16-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/USC/014122	International filing date (day/month/year) 23 MAY 2000	Priority date (day/month/year) 24 MAY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 15/10, 15/62, 15/64; C12P 21/02 and US Cl.: 435/69.1, 91.42; 536/23.4		
Applicant NEW ENGLAND BIOLABS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
- ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 17 NOVEMBER 2000	Date of completion of this report 23 AUGUST 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer TERRY A. MCKELVEY 
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/14122

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed☒ the description:

pages (See Attached) _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

☒ the claims:

pages (See Attached) _____, as originally filed
 pages _____, as amended (together with any statement) under Article 19
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

☒ the drawings:

pages (See Attached) _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

☒ the sequence listing part of the description:

pages (See Attached) _____, as originally filed
 pages _____, filed with the demand
 pages _____, filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.☒ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig. NONE5. ☐ This report has been drawn up as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/14122

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims <u>9-11, 14-15, 17-20, and 22-32</u>	YES
	Claims <u>1-8, 12-13, 16, and 21</u>	NO
Inventive Step (IS)	Claims <u>9-11, 14-15, 17-20, and 22-32</u>	YES
	Claims <u>1-8, 12-13, 16, and 21</u>	NO
Industrial Applicability (IA)	Claims <u>1-32</u>	YES
	Claims <u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-8, 12-13, 16, and 21 lack novelty under PCT Article 33(2) as being anticipated by Comb et al.

Comb et al teach splitting DNA coding for a target protein into fragments encoding the protein and inserting a DNA encoding a fragment of a controllable intervening protein sequence onto each terminus (C-terminus to N-terminus as appropriate for the target protein to be reconstituted by intein-mediated trans-splicing), thereby separating the DNA fragments so that the target protein is expressed in two fragments, each fragment comprising a part of a controllable intervening protein sequence. The target protein is then reconstituted from the expressed fragments (columns 16-18). Although this reference does not specifically teach that the purpose of the splitting of the DNA coding for the target protein followed by separating the DNA fragments is to prevent transmission to other organisms of the gene coding for the target protein, the steps that comprise the claimed method are all taught and thus the method taught by the reference would inherently result in preventing transmission as claimed. This reference teaches that the organism that the protein is expressed in can be *E. coli* (columns 16-17). The DNA molecule that the DNA fragments can be inserted into are taught as being any of DNA from a virus, plasmid, etc (columns 15-16).

Claims 9-11, 14-15, 17-20, and 22-32 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest compartmentizing each DNA fragment into separate specified cell compartments, use of protein complementation for reconstitution, analyzing the primary amino acid sequence of the target protein by specific methods in order to determine a potential split site, or specific isolated DNA fragments.

Claims 1-32 meet the criteria set out in PCT Article 33(4), for industrial applicability.

----- NEW CITATIONS -----
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/14122

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-72 and 74-93, as originally filed.
page(s) 72, filed with the demand,
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) 96-99, as originally filed.
page(s) NONE, as amended under Article 19.
page(s) NONE, filed with the demand,
and additional amendments:
NONE

This report has been drawn on the basis of the drawings,
page(s) 1-33, as originally filed.
page(s) NONE, filed with the demand,
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) 1-41, as originally filed.
pages(s) NONE, filed with the demand,
and additional amendments:
NONE

*** RX REPORT ***

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